THE THERAPEUTIC EFFECT OF MELATONIN ON CANINE MELANOSIS

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The pigmentation of animal skin is controlled by the relative dispersion or aggregation of melanin within the melanocyte. It has been postulated by Lerner (1) that this balance is maintained by the pituitary-pineal axis in the following manner (see Fig. 1):

1. The dispersion of melanin, with a consequent darkening of the skin is induced by the melanocyte-stimulating hormone, alpha MSH, produced by the pituitary gland (2, 3). This could be called the melanoid effect.

2. The aggregation of melanin and lightening of the skin is brought about by N acetyl-5-methoxytryptamine, melatonin, which is produced by the pineal gland (3, 4). This could be called the lucific effect.

Alpha MSH and melatonin are the most active agents known; however, there may be other compounds which are involved in this phenomenon and which are produced in the pineal body and the pituitary gland. It has been shown that the melanoid effect in man can be induced by the administration of alpha MSH (5) but the lucific effect, due to melatonin, has only been demonstrated in amphibia at this time.

In pathological pigmentation in man (*e.g.* Addison's disease) there is an increased level of MSH due to the overproduction of pituitary trophic hormones to compensate for adrenal insufficiency (6). Assuming that similar changes take place in the various melanotic conditions seen in dogs, it was theorized that pineal agents such as melatonin should act as lucifics and be as effective as therapeutic agents in these cases.

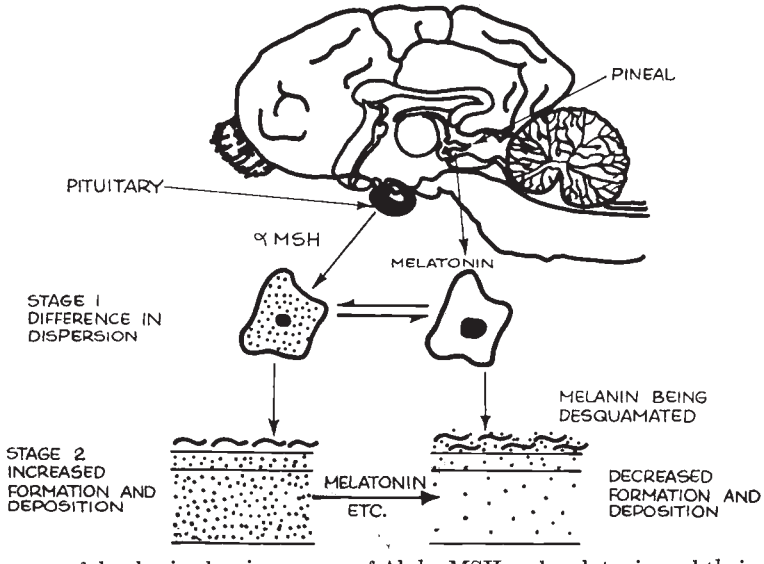

FIG. 1. Diagram of dog brain showing source of Alpha MSH and melatonin and their effects on melanocytes and skin.

Melanosis in dogs frequently accompanies a variety of dermatoses including those associated with non-specific allergies, hormonal disturbances and chronic inflammation. Melanosis can occur locally at the site of an inflammatory lesion, such as in the cornea, ear flap, foot, vulva, etc.; or it is seen bilaterally in cases of alopecia where it involves the axilla, groin and flank. It is also found in advanced chronic cases from various causes, and in these circumstances it may be diffuse and general. In some of the more severe cases the skin becomes grossly thickened (hyperkeratosis) with heavy pigmen-

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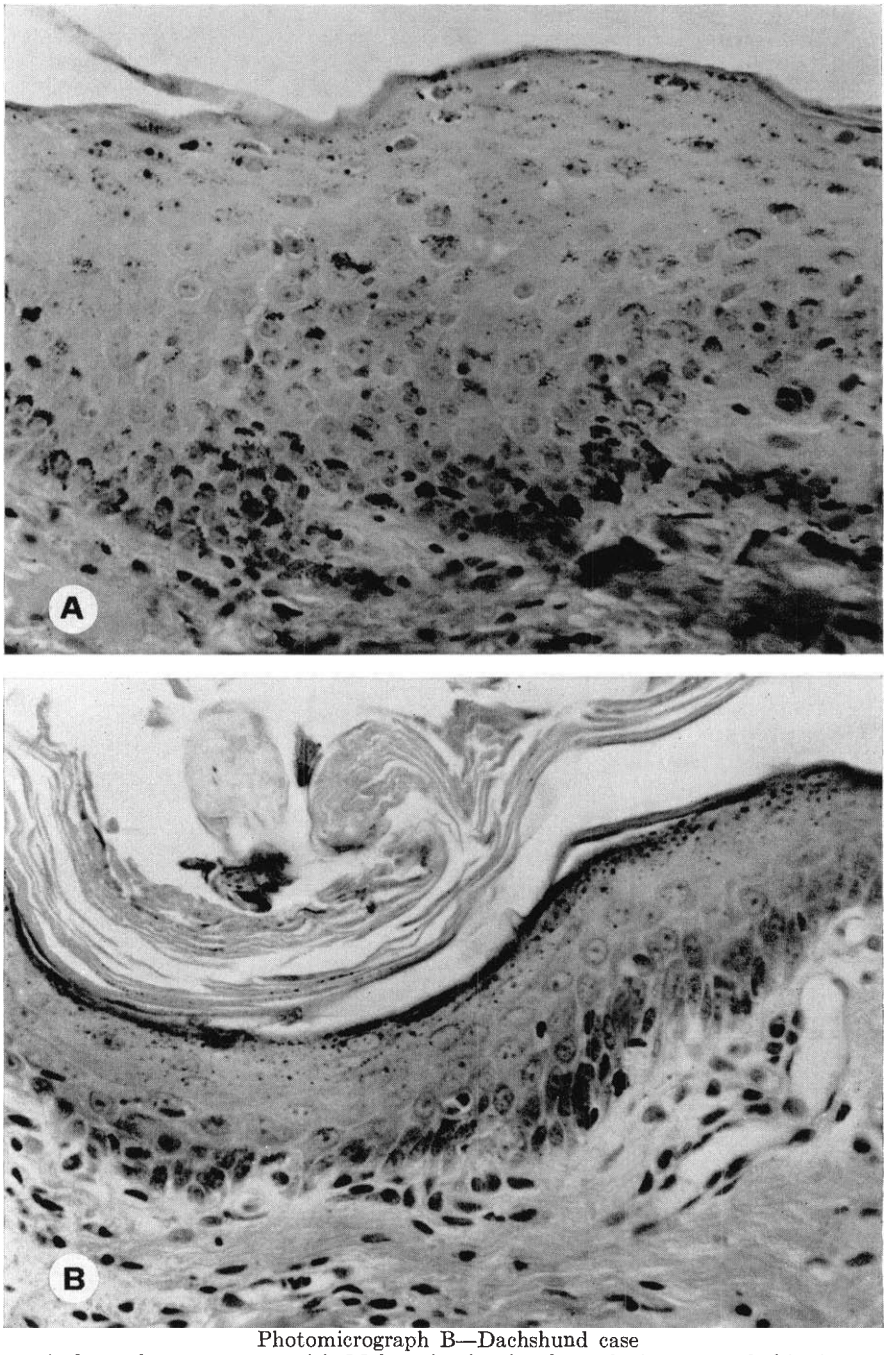
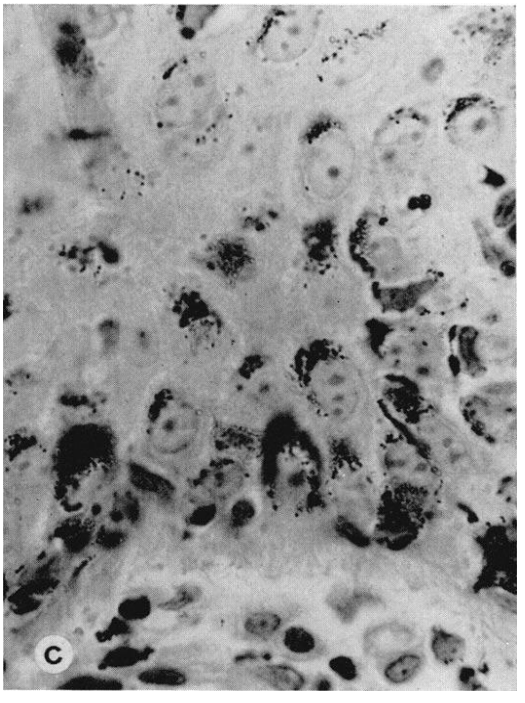
Photomicrograph A—Dachshund case
Section of skin from Axilla H and E stain × 400



Photomicrograph B—Dachshund case
7 days after treatment with Melatonin showing loss of pigment and thinning of Malpighian layer

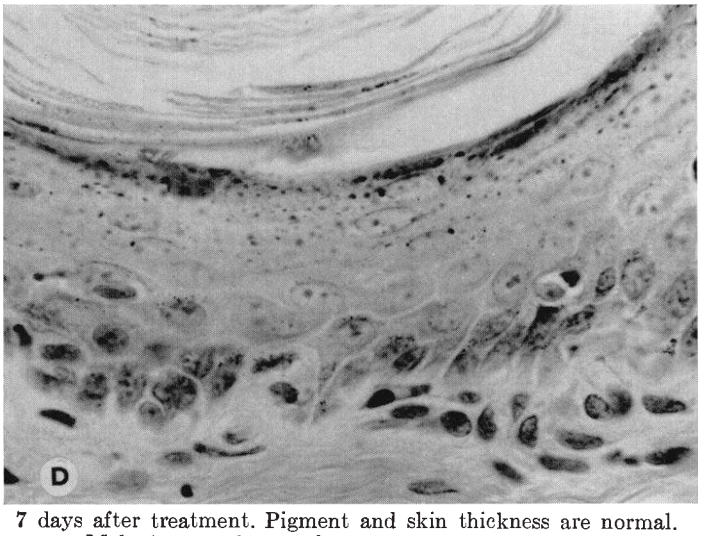
FIG. 2. Photomicrograph of melanotic skin before and after treatment with melatonin.

Photomicrograph C
Dachshund case
Section of skin
from axilla
H & E stain
× 840



Before treatment—a typical field showing heavy pigmentation at the base of the Malpighian layer
See legend facing page

Photomicrograph D
Dachshund case



7 days after treatment. Pigment and skin thickness are normal. Melanin granules can be seen in stratum corneum
See legend facing page

tation and follicular plugging. Canine melanoses are commonly known to veterinarians as "acanthosis nigricans" although they do not fully correspond to the human condition of the same name. In man, acanthosis nigricans is nearly always concomitant with a malignancy, while in the dog this is rarely the case.

The current theory to explain the phenomenon of melanosis in dogs is based on thyroid dysfunction (7). The recommended treatment is to inject thyroid-stimulating hormone (TSH) which results in a temporary skin lucification. The action of TSH in these cases is not fully understood but presumably it brings about an increased production of thyroxin and tri-iodothyronine which are known to have a lightening effect on the melanocyte (8). Since it has been shown (1) that melatonin is 10,000 times more potent than tri-iodothyronine, it was anticipated that melantonin would prove to be more effective therapeutically in canine melanoses.

METHOD

Three dogs with advanced symptoms of melanosis were selected for treatment. The first two cases —a spayed cocker spaniel, 8 yrs and 30 lbs and a male dachshund, 4 yrs and 25 lbs—showed heavy pigmentation and chronic thickening of the skin generally. This was especially noticeable in the axilla and groin. The third case, a female wire haired fox terrior, 7 yrs and 16 lbs, had melanotic otitis and blepharitis on the right side only. This condition was associated with a low-grade infection of the ear and eye. The chronic inflammation was perpetuated by frequent scratching.

Each dog was given 1 mg of *N* acetyl-5-methoxytryptamine subcutaneously for three consecutive days. Photographs were made of the first two cases and biopsy specimens were taken of the skin. The third case in addition was treated with antibiotics and steroids locally, but no biopsy studies were made.

RESULTS

The response was dramatic. In all cases there was a visible lightening of the melanotic areas which could be detected macroscopically within 48 hours. Dark scales from the skin indicated that melanin deposits were being desquamated. Later biopsy specimens disclosed that melanin was in fact being extruded (see Fig. 2).

Within one week the affected skin had resumed a thinner and more pliable consistency. Subsequent treatment with steroids seem to enhance the original action. The rapid lightening was possibly due to immediate aggregation of melanin.

These findings agree with the hypothesis that pathological pigmentation is under the control of the pituitary-pineal axis and that this balance can be altered by increasing the pineal content. Melatonin appears to be of value as a lucific in the treatment of melanoses and related conditions. It is believed that it will also be useful when combined with antibiotics and steroids in the treatment of inflammation and infection where melanosis is a concomitant problem. At this time a study or more than 100 dogs is being completed in order to determine the prophylactic and therapeutic applications of melatonin and other pineal agents in veterinary practice.

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